

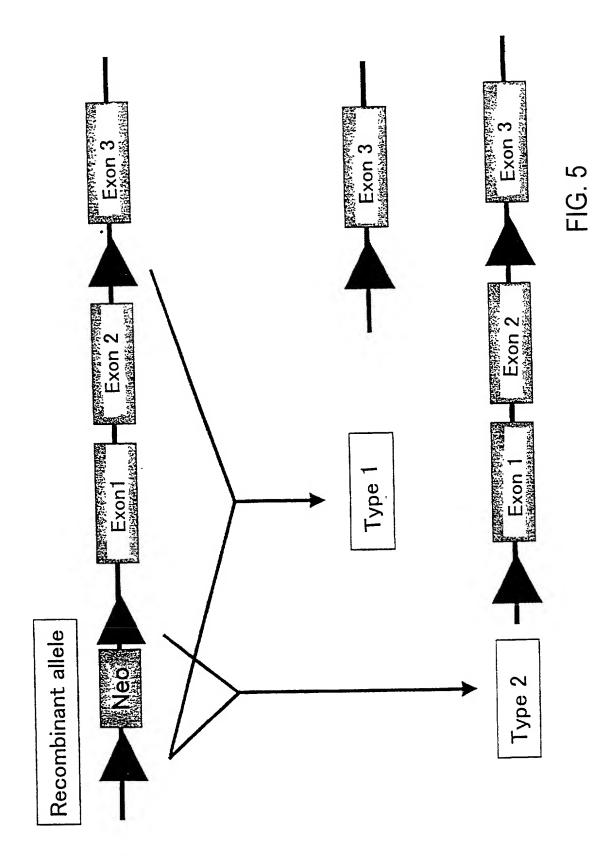
GGAGATCCAGCTGCTGCGGCGGCTGCGGCATCGGAATGTGATCCAGCTTGTGGACGTGCTGTACAATGAGGAGAAGCAGA AGATatatcctgtgggtggagtgggctggggtggcccctgtgttaggggctggaagccttctgcaaggcctctggcagca cctgttctgagcagtgtggctgggactgggcatggcctcacagggacttggggcctatgtacattgacagggccccggct ggttctagaggtttccatgctgccccttcccagaggtagaggttgcacagcctacgttgcatctgggcagtcctgggagc attotgagaacccagtgccctgcagccccaactcctggtacccatctctccctgtggctagtacaccagctgatttcagt cctgttgtaatctatgctgactccatgtggtccaagtcactgtggtggtcttgtggaccctgtgagtactgatagggagc gcagaatggcgggagagcagagtggtggtgtctgttggcccagcggggccctccagaccactgttgctaggagcagggc  $\tt CTGGACAGTGTGCCGGAGAAGCGCTTCCCTGTGTGCCAAGCTCATGGgtgagtgccctgctggtgcaggaggagcagcc$  ${\tt attgtcaggaaacccaggtgtttctgggcccccagtttttaacccagccaatgtgcttagggttaccctcttgttaggcc}$ ctgtggtcccgctgccctgcagagccatagtgggtctgagtcctgttcagtgctcccaggttcagcagaatcacatcccc tgactgccagttgccctgtgtaattttagtggcccagccttctgactctcaggtctgtttgcctgagccctaaacatcta tcaccttgtaggccaggtctcatgagtctcccaaacttcatatcagacttatgtaggtaccatggtatgggctgagacac ATTGTTCACAAGGACATCAAGCCGGGCAACCTGCTACTCACCACCAATGGCACACTCAAGATCTCCGACCTCGGTGTTGC CCTTTCGCTGTGGATGACACCTGCCGGACAAGCCAGGGCTCCCCGGCCTTCCAGCCTCCTGAGATTGCCAATGGACTGGA CACCTTTTCAGGTTTCAAGGTGGACATCTGGTCAGCTGGGGTCACACTgtaagtgtcttgtgtgtaccctgtagcagatg gggggctgtgggttttccctagtgttcttgggcctttttgcccacagtgtgtggctagcaggttggacattccaggtctg ctaccagttaacatgtgtcctgtctgggagttggggcacctgtcctctggtctccagtgtggccagcactgacactcttt tcctatgtgaagTTACAACATCACCACGGGCCTGTACCCATTTGAGGGGGGACAATATCTACAAGCTCTTTGAGAACATTG GGAGAGGAGACTTCACCATCCCTTGTGACTGCGGCCCACCACTCTCTGACCTACTCCGAGgtgggcatctctaaatcacc canatgttaggacagcaagggacagagcccttggtctggaggggttctgaccttactgtcaggacagcctttgtccgcca ctcagcctgctgggggtctgagctgagaacatggtctcagaggtgctaggtcatcacaggagtaaggatcagtgtgctgt gtgtattgatgtctgggaaggctgtgtgtgaacttggggtgtgacaggggtgcccaatgcaggcctccctacctttatca ttttgttcaggagtgcaggcgttatgtggcctgagaagctgtagatttcagggcctagaattagagacggatcctcccat ggtgggggggggggggggagtgggaagtgtcactttggatcccagctgttccttggccatctggacatggaaatgtgtc Appln No.: 10/006,611

Applicant(s): Jun-ichi Nezu et al. LKB1 GENE KNOCKOUT ANIMALS

tagggaggccaacaggaagcgtgaggcatggtgtctttcctcacctgaggctaagagccttctgggtaacagtggagcctctgtcctccctttgtttatttaccagctggtcagagcctttgggtccaggcttctctgtcctcttctcccttcatgctag act gag act ggc t cag ct ggg t gt cccc cag t gag ggc t t ctag cct at ccg t gt t caa gg cgg gt ggg act at ag gt gctaggetacct caage ctg tag ccg gag cacta aggect cgt cttat gtaag gac ag ccat gg tg tg gg ctt tg gt gg gt aggect cat gg tg taggect tagget gag gac agg cat gag gag cacta gg tg tagg gag cacta gg tagg gag $\tt ttggccagccgtggtcacagtgcctggcacctgatgtctgtgctgcacttggccttctttagCTGGTTCCGGAAGAAACA$ CCCTCTGGCTGAGGCGCTCGTACCTATCCCACCAAGCCCAGACACTAAGGACCGCTGGCGCAGTATGACTGTAGTGCCCT ACCTGGAGGACCTGCATGGCCGTGCGGAGGAGGAGGAGGAGGAGGAGGACTTGTTTGACATTGAGGACGGCATTATCTACACC ${\tt CAGGACTTCACAGTGCCTGgtaagctggcttggcgcagctcctactggagctggtgactttgtgcactctggggctggtc}$ cccttcccaagtctccagccagctaacatgagccaccaggactgccaaagccatcctggtggctgtggcatttcactctg ggctagatgaagggctccctggctgcatctagcaggaggaggggaaccctggagggcagtgggtaggggccctgagacag ccacctgagggagggtccagtggccctcggtcctggccatgcctgaccttatatcgccttcttccccaggtgtcgaggag tgtctgcaggtggatgcttgccgcgacttccctcctgtcactaccctgacaggctccccaccagggtttcagagaacatgcctgcatgccagtcccacttagctcctggcctttcaaatagctttggtgggagggtaaggaccttgggctactgtgtctc ctgtagcaattgagagttctaatagcagtgcccgctgggtgccaggtggaatccacaaggacaggtatacacctgatgtc cagtatgggccttggccacagccctttctaaggtttaaagcatccctatgtgggaatagtgtcttctactctgtcacgtg gagcccttgtctagactgtcccacaggctgggctcctggctgagagctggtttctctgctggggagaagatgtacttagg  $\verb|cccatttgtcaaatggggtagtgttgcacagagtgaagtgaccgtgctctgaggatagcctgatccctctgtacttggca|\\$ tgagggtcggactctgcagcaacaggacaggggctttctactcagtgccttgtgtggaggaggggacagatgctttctcagagtccacctgacctcaagcctcagtcccatgcagagtgagccagagtgggtgctgctagtgtggccaagtcagagggtt tgtggagttacatgtagacactgacctctggagcctgggaagcttcaggagaggccatcttttgtcccactgcgagggca ggccaacagagcaagctggtctgcagccctcagctggatgatctccttcccggtgctcatcgcagctagtagctcccagg  ${\tt ccgaatgcttcatctccttgtgcctgtactgagggtctagagcctctcccttggagagctctgtgagctggtgctgggct}$ gcccaggctagacaggcaggtgagcgtgggcatgctgcaggagggccagggcatagcactgtgaaggcagtgggcctgct tgggccctggggctttgagctacctgccccttggctcaagctatgcttgccatcttcccgtagGACAGGTCCTGGAAGAG GAAGTGGGTCAGAATGGACAGAGCCACAGTTTGCCCAAGGCTGTTTGTGTGAATGGCACAGAGCCCCAGCTCAGCAGCAA GGTGAAGCCAGAAGGCCGACCTGGCACCGCCAACCCTGCGCGCAAGGTGTGCTCCAGCAACAAGATCCGCCGGCTCTCGG CCTGCAAGCAGCAGTGACTGAGGCCTACAGgtgggcatgggcctgggtccagccatccctggtgttcacagtgggtgtct gctgggctcctagctccttcccgtagggcagtgctgcaagggggaaggtctggtggttgaggtggtactaagtgaccacc 

CTATCTTTTGGCAATAAATAAAGCTTGGGAAACTTG

FIG. 4



က် ည်

HindIII Xhol

loxP ->

BamHI

Ecori

Appln No.: 10/006,611 Applicant(s): Jun-ichi Nezu et al. LKB1 GENE KNOCKOUT ANIMALS

F23 synthetic linker

က် tgcgacacatogataccgctogagtcg ည်

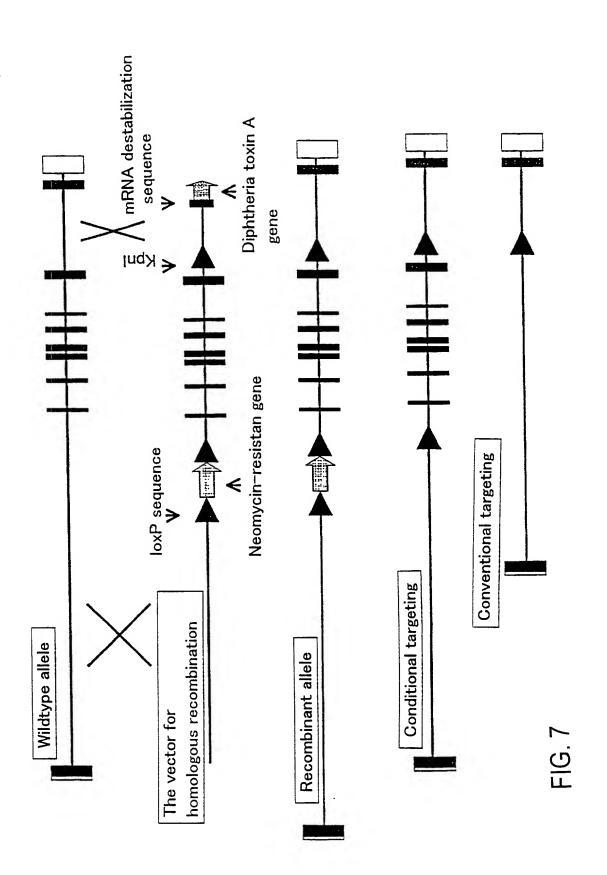
ည acglacgetgtagetatggcgagetgagettaa က်

EcoRI XhoI ClaI Avalll

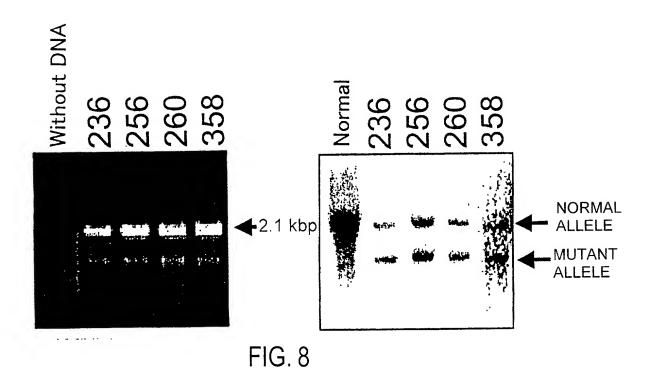
loxP2 synthetic linker

ctagicaagotteataactfegtataggatacattataegaagitategaattegacetggategeataactegtatageatatatagaagutateaagetteg Spel HindIII ည်

asticgaastattgaagcatatogtatglaatatgottcaatagcttaagctgsactaggstattgaagcatatcstatglaatatgoffcaatagttogaaggaggag က်





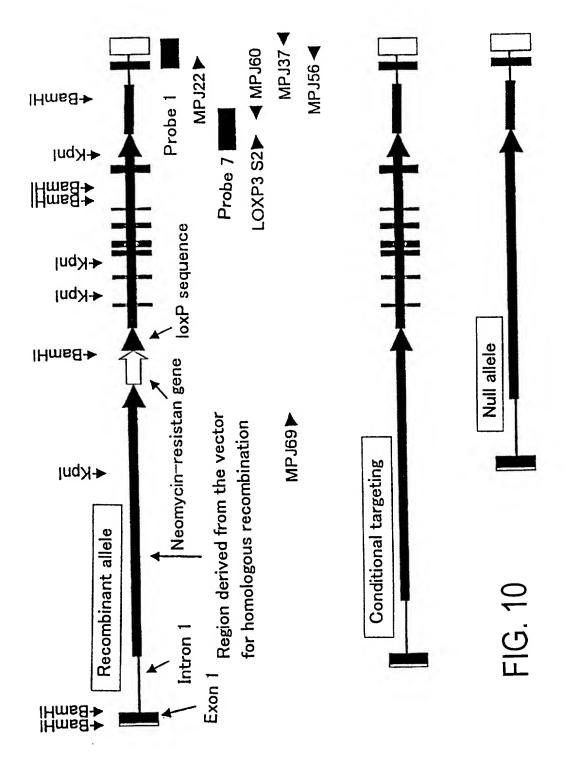


Normal/Mutant

82 92 25 25 4 Normal allele

Mutant allele

FIG. 9



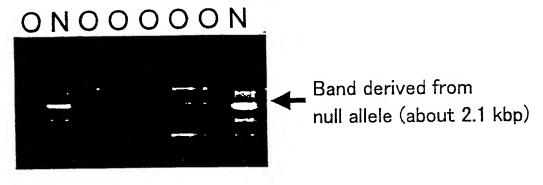


FIG. 11A

